

wherein  $R^1$  represents H or alkyl of 1 - 3 carbons; and

each T represents a substituent group, independently selected from the group consisting of:

- \* the halogens -F, -Cl, -Br, and -I;
- \* alkyl of 1 - 10 carbons;
- \* haloalkyl of 1 - 10 carbons;
- \* haloalkoxy of 1-10 carbons;
- \* alkenyl of 2 - 10 carbons;
- \* alkynyl of 2 - 10 carbons;
- \*  $-(CH_2)_pQ$ , wherein
  - p is 0 or an integer 1 - 4,
- \* -alkenyl-Q, wherein
  - said alkenyl moiety comprises 2 - 4 carbons; and
- \* -alkynyl-Q, wherein
  - said alkynyl moiety comprises 2-7 carbons; and

Q is selected from the group consisting of aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, -CN, -CHO, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>2</sup>, -OCOR<sup>2</sup>, -SOR<sup>3</sup>, -SO<sub>2</sub>R<sup>3</sup>, -CON(R<sup>4</sup>)<sub>2</sub>, -SO<sub>2</sub>N(R<sup>4</sup>)<sub>2</sub>, -C(O)R<sup>2</sup>, -N(R<sup>4</sup>)<sub>2</sub>, -N(R<sup>2</sup>)COR<sup>2</sup>, -N(R<sup>2</sup>)CO<sub>2</sub>R<sup>3</sup>, -N(R<sup>2</sup>)CON(R<sup>4</sup>)<sub>2</sub>, -CHN<sub>4</sub>, -OR<sup>4</sup>, and -SR<sup>4</sup>;

wherein

R<sup>2</sup> represents H;

alkyl of 1 - 6 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R<sup>3</sup> represents alkyl of 1 - 4 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R<sup>4</sup> represents H;

alkyl of 1 - 12 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons;

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

alkenyl of 2 - 12 carbons;

alkynyl of 2 - 12 carbons;

$-(C_qH_{2q}O)_rR^5$  wherein q is 1-3; r is 1 - 3; and  $R^5$  is H provided q is greater than 1, or alkyl of 1 - 4 carbons, or phenyl;

alkylenethio terminated with H, alkyl of 1-4 carbons, or phenyl;

alkyleneamino terminated with H, alkyl of 1-4 carbons, or phenyl]

$-(CH_2)_sX$  wherein s is 1 - 3 and X is halogen;

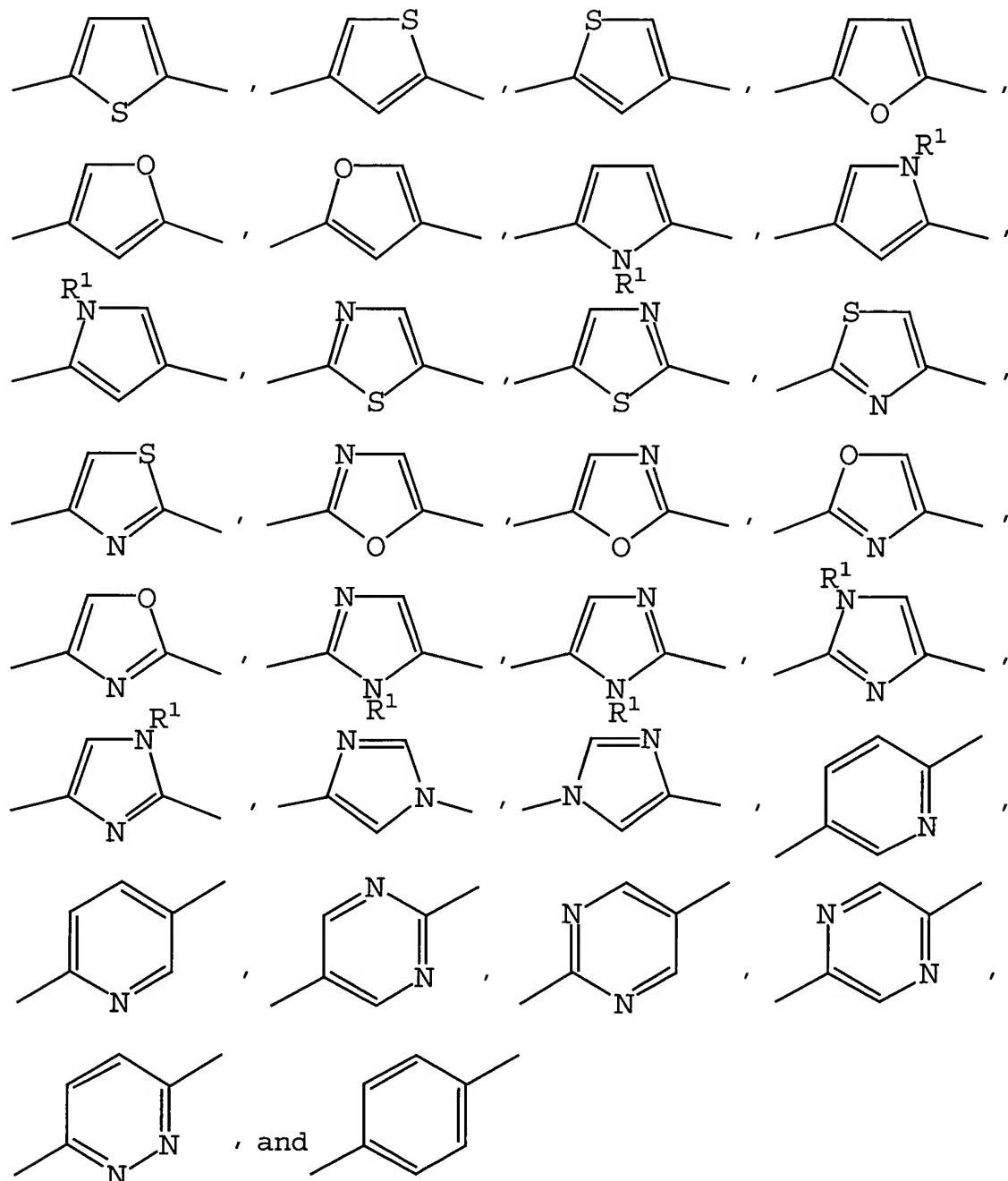
$-C(O)OR^2$ ; or

$-C(O)R^2$ ;

and with the provisos that a) when two  $R^4$  groups are situated on a nitrogen, they may be joined by a bond to form a heterocycle, and b) unsaturation in a moiety which is attached to Q or which is part of Q is separated from any N, O, or S of Q by at least one carbon atom, and

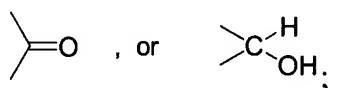
x is 0, 1, or 2;

(b) B represents a bond or an optionally substituted aromatic or heteroaromatic ring containing 0-2 substituents T, which substituents T may independently have the meaning specified under (a), the B rings being selected from the group consisting of:



wherein  $R^1$  is as defined above; and each  $R^1$  may be the same or different:

(c) D represents



(d) E represents a chain of n carbon atoms bearing m substituents R<sup>6</sup>, wherein said R<sup>6</sup> groups are independent substituents, or constitute spiro or nonspiro rings in which a) two groups R<sup>6</sup> are joined, and taken together with the chain atom(s) to which said two R<sup>6</sup> group(s) are attached, and any intervening chain atoms, constitute a 3 - 7 membered ring, or b) one group R<sup>6</sup> is joined to the chain on which said one group R<sup>6</sup> resides, and taken together with the chain atom(s) to which said R<sup>6</sup> group is attached, and any intervening chain atoms, constitutes a 3 - 7 membered ring; and wherein

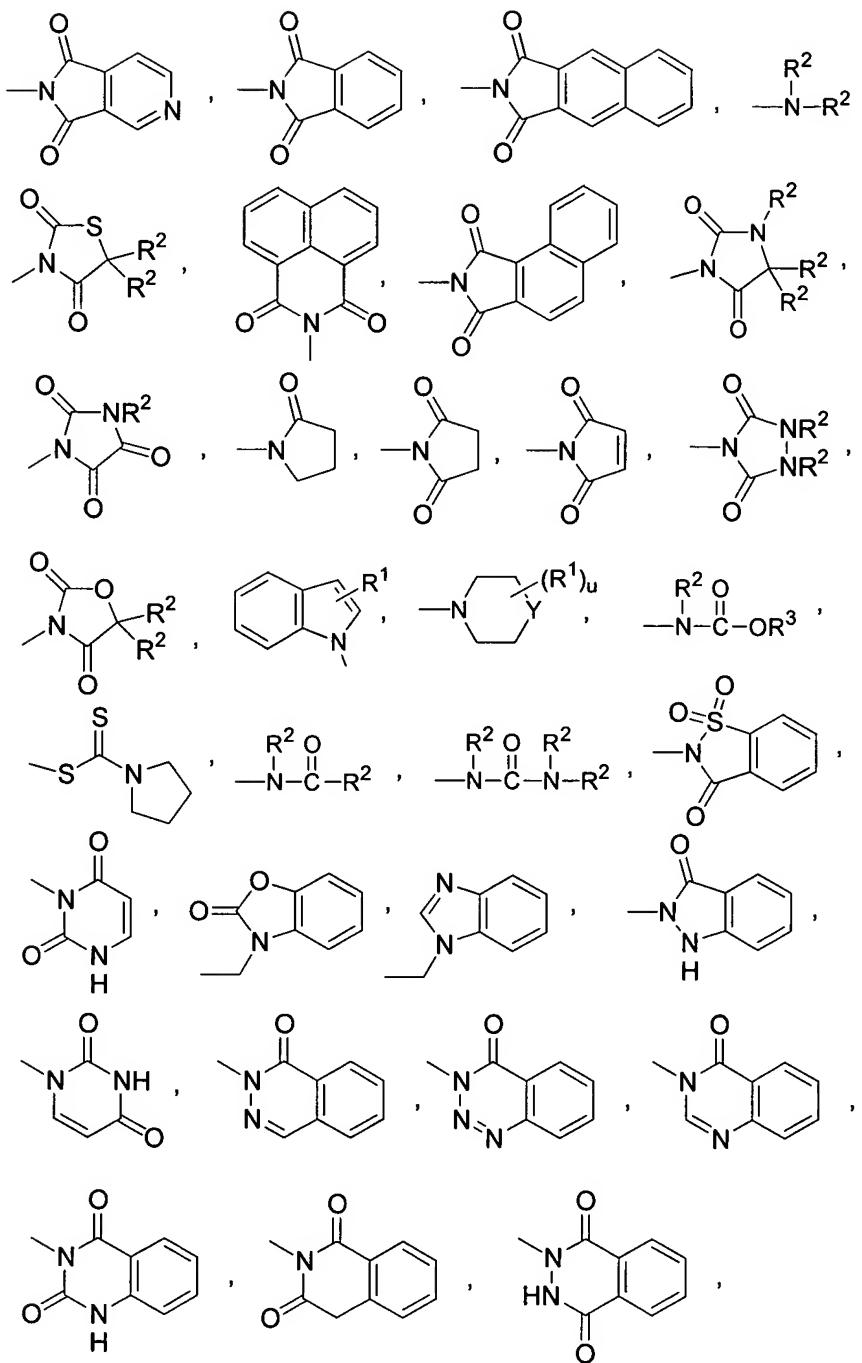
n is 2 or 3;

m is an integer of 1 - 3;

each group R<sup>6</sup> is independently selected from the group consisting of:

- \* fluorine;
- \* hydroxyl, with the proviso that a single carbon may bear no more than one hydroxyl substituent;
- \* alkyl of 1 - 10 carbons;
- \* aryl of 6 - 10 carbons;
- \* heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;
- \* arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;
- \* heteroaryl-alkyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 8 carbons;
- \* alkenyl of 2 - 10 carbons;
- \* aryl-alkenyl wherein the aryl portion contains 6 - 10 carbons and the alkenyl portion contains 2 - 5 carbons;
- \* heteroaryl-alkenyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkenyl portion contains 2 - 5 carbons;
- \* alkynyl of 2 - 10 carbons;

- \* aryl-alkynyl wherein the aryl portion contains 6 - 10 carbons and the alkynyl portion contains 2 - 5 carbons;
- \* heteroaryl-alkynyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkynyl portion contains 2 - 5 carbons;
- \*  $-(CH_2)_tR^7$  wherein  
t is 0 or an integer of 1 - 5; and  
 $R^7$  is selected from the group consisting of



and corresponding heteroaryl moieties in which the aryl portion of an aryl-containing R<sup>7</sup> group comprises 4 - 9 carbons and at least one N, O, or S heteroatom;

wherein

Y represents O or S;

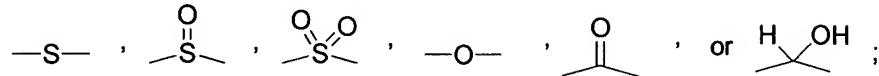
$R^1$ ,  $R^2$ , and  $R^3$  are as defined above; and each  $R^1$ ,  $R^2$  or  $R^3$  may be the same or different; and

$u$  is 0, 1, or 2; and

\*  $-(CH_2)_vZR^8$  wherein

$v$  is 0 or an integer of 1 to 4; and

$Z$  represents



$R^8$  is selected from the group consisting of:

alkyl of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion contains 6 to 10 carbons and the alkyl portion contains 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$-C(O)R^9$  wherein  $R^9$  represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion contains 6 - 10 carbons or is heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 4 carbons;

and with the provisos that

- when  $R^8$  is  $-C(O)R^9$ ,  $Z$  is S or O;

- when  $Z$  is O,  $R^8$  may also be  $-(C_qH_{2q}O)_rR^5$  wherein  $q$ ,  $r$ , and  $R^5$  are as defined above; and

\*  $-(CH_2)_wSiR^{10}3$  wherein

$w$  is an integer of 1 to 3; and

$R^{10}$  represents alkyl of 1 to 2 carbons;

and with the proviso that

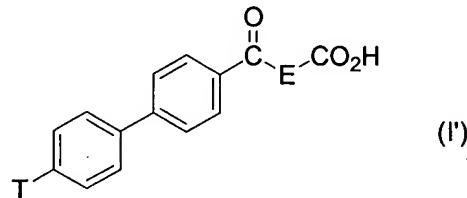
- aryl or heteroaryl portions of any of said T or R<sup>6</sup> groups optionally may bear up to two substituents selected from the group consisting of -(CH<sub>2</sub>)<sub>y</sub>C(R<sup>4</sup>)(R<sup>3</sup>)OH, -(CH<sub>2</sub>)<sub>y</sub>OR<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>SR<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>S(O)R<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>S(O)R<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>SO<sub>2</sub>N(R<sup>4</sup>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>y</sub>N(R<sup>4</sup>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>y</sub>N(R<sup>4</sup>)COR<sup>3</sup>, -OC(R<sup>4</sup>)<sub>2</sub>O- in which both oxygen atoms are connected to the aryl ring, -(CH<sub>2</sub>)<sub>y</sub>COR<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>CON(R<sup>4</sup>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>y</sub>CO<sub>2</sub>R<sup>4</sup>, -(CH<sub>2</sub>)<sub>y</sub>OCOR<sup>4</sup>, -halogen, -CHO, -CF<sub>3</sub>, -NO<sub>2</sub>, -CN, and R<sup>3</sup> wherein

y is 0 - 4; and

R<sup>3</sup> and R<sup>4</sup> are as defined above, and each R<sup>3</sup> and R<sup>4</sup> may be the same or different; and any two R<sup>4</sup> which are attached to one nitrogen may be joined to form a heterocycle;

or a pharmaceutically acceptable salt or prodrug thereof.

2. (Amended) The method according to claim 1 wherein the method comprises administering a compound of the general formula (I')

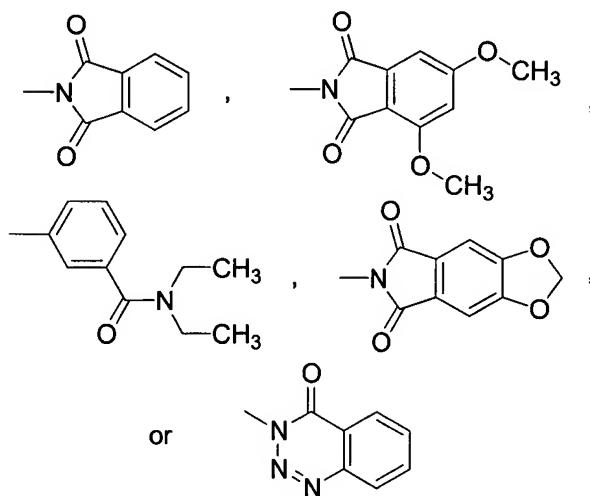


wherein

T is (C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy, chloride, bromide, fluoride, acetoxy, hydroxy, cyano, trifluoromethyl or trifluoromethoxy,

CO-E-CO<sub>2</sub>H represents a 3-carboxyl-5-(R<sup>7</sup>)-pentan-1-on-1-yl- or a [2-carboxyl-3-(R<sup>7</sup>)-methyl-cyclopentan-1-yl]-carbonyl-residue, wherein

R<sup>7</sup> represents a group of the formula



or a salt thereof.

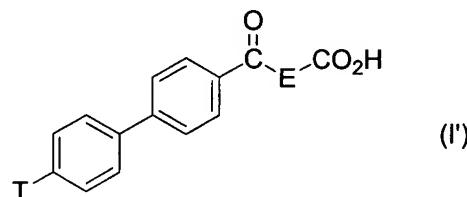
3. (Amended) The method according to claim 2, characterized in that one enantiomer of a pair of enantiomers at a chiral center adjacent to the carboxylic acid moiety of the group of the formula  $\text{CO}-\text{E}-\text{CO}_2\text{H}$  in compounds of the general formula (I') more potently inhibits MMP-2 and/or MMP-9.

4. (Amended) The method according to claim 1, wherein the compound is selected from the group consisting of

(+)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-(4'-ethoxyl[1,1'-biphenyl]-4-yl)-4-oxobutanoic acid,  
 (+)-4-(4'-chloro[1,1'-biphenyl]-4-yl)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-oxobutanoic acid,

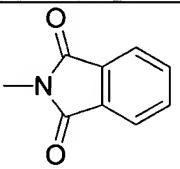
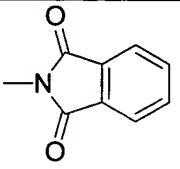
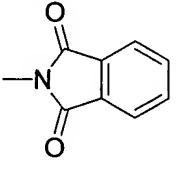
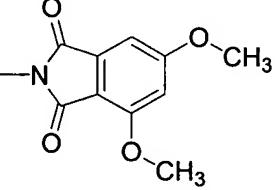
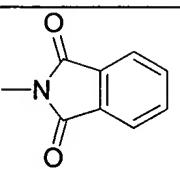
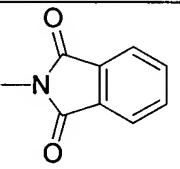
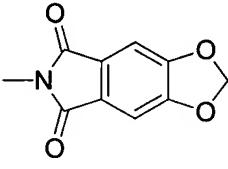
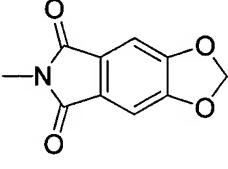
and salts thereof.

5. (Amended) A compound of the general formula (I'),



wherein  $\text{CO}-\text{E}-\text{CO}_2\text{H}$  represents a 3-carboxyl-5- $\text{R}^7$ -pentan-1-on-1-yl residue, and wherein T and  $\text{R}^7$  have the meaning indicated in the following table:

T	$\text{R}^7$	racemate, (+)- or (-)-enantiomer	
OEt		(+)	;

OEt		(-)	;
OAc		rac	;
OH		rac	;
C1		rac	;
Br		(+)	;
Br		(-)	;
C1		(+)	;
C1		(-)	;